Sequence Range: 1 to 494

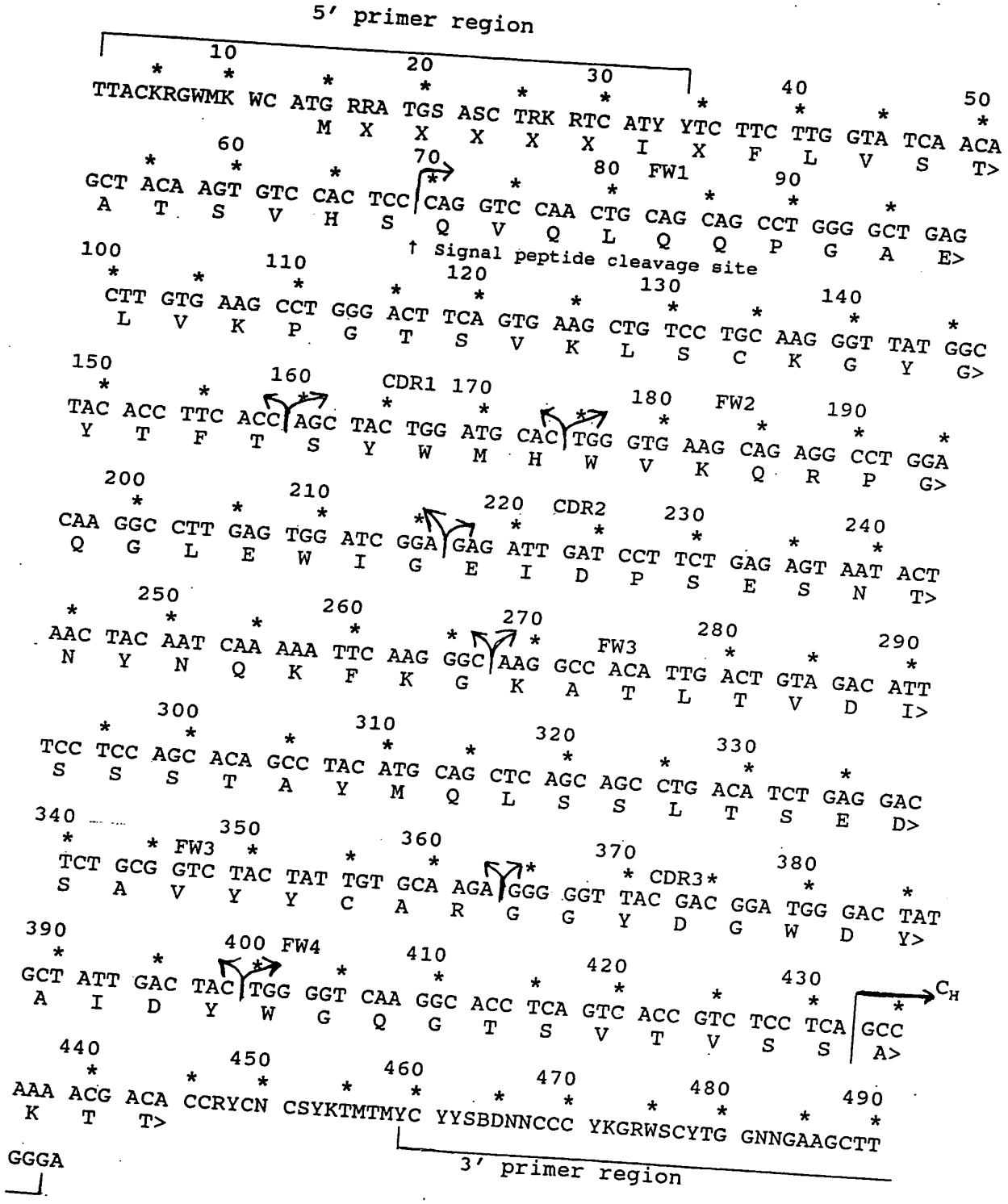

FIG. 1

Sequence Range: 1 to 428

```
                10                  20                  30                  40                  50
TTACTTGACG ACTCGGG ATG GGA TGG AGC TAT ATC ATC TTC TTC TTG GTA TCA
                    M   G   W   S   Y   I   I   F   F   L   V   S>

        60                  70                  80                  90                  100
ACA GCT ACA AGT GTC CAC TCC CAG GTC CAA CTG CAG CAG CCT GGG GCT
T   A   T   S   V   H   S   Q   V   Q   L   Q   Q   P   G   A>

        110                 120                 130                 140
GAG CTT GTG AAG CCT GGG ACT TCA GTG AAG CTG TCC TGC AAG GGT TAT
E   L   V   K   P   G   T   S   V   K   L   S   C   K   G   Y>

150                 160                 170                 180                 190
GGC TAC ACC TTC ACC AGC TAC TGG ATG CAC TGG GTG AAG CAG AGG CCT
G   Y   T   F   T   S   Y   W   M   H   W   V   K   Q   R   P>

200                 210                 220                 230                 240
GGA CAA GGC CTT GAG TGG ATC GGA GAG ATT GAT CCT TCT GAG AGT AAT
G   Q   G   L   E   W   I   G   E   I   D   P   S   E   S   N>

        250                 260                 270                 280                 290
ACT AAC TAC AAT CAA AAA TTC AAG GGC AAG GCC ACA TTG ACT GTA GAC
T   N   Y   N   Q   K   F   K   G   K   A   T   L   T   V   D>

        300                 310                 320                 330                 340
ATT TCC TCC AGC ACA GCC TAC ATG CAG CTC AGC AGC CTG ACA TCT GAG
I   S   S   S   T   A   Y   M   Q   L   S   S   L   T   S   E>

        350                 360                 370                 380
GAC TCT GCG GTC TAC TAT TGT GCA AGA GGG GGT TAC GAC GGA TGG GAC
D   S   A   V   Y   Y   C   A   R   G   G   Y   D   G   W   D>

390                 400                 410                 420
TAT GCT ATT GAC TAC TGG GGT CAA GGC ACA TCA GTC ACC
Y   A   I   D   Y   W   G   Q   G   T   S   V   T>
```

FIG. 2

App No.: 08/700,737
Title: "Humanized Immunoglobulin ..."
Inventors: Paul D. Ponath, *et al.*

```
Sequence Range:  1 to 535

                              5' primer region
             10          20          30          40                    50
CGATTACTAG TCGAC ATG AAG TTG CCT GTT AGG CTG TTG GTG CTT CTG TTG
                  M   K   L   P   V   R   L   L   V   L   L   L

                                              Signal peptide cleavage site
        60          70                    80          90
TTC TGG ATT CCT GTT TCC GGA GGT↓GAT GTT GTG GTG ACT CAA ACT CCA
 F   W   I   P   V   S   G   G   D   V   V   V   T   Q   T   P>

100         110         120         130         140
CTC TCC CTG CCT GTC AGC TTT GGA GAT CAA GTT TCT ATC TCT TGC AGG
 L   S   L   P   V   S   F   G   D   Q   V   S   I   S   C   R>

150         160         170         180         190
TCT AGT CAG AGT CTT GCA AAG AGT TAT GGG AAC ACC TAT TTG TCT TGG
 S   S   Q   S   L   A   K   S   Y   G   N   T   Y   L   S   W>

200         210         220         230         240
TAC CTG CAC AAG CCT GGC CAG TCT CCA CAG CTC CTC ATC TAT GGG ATT
 Y   L   H   K   P   G   Q   S   P   Q   L   L   I   Y   G   I>

       250         260         270         280         290
TCC AAC AGA TTT TCT GGG GTG CCA GAC AGG TTC AGT GGC AGT GGT TCA
 S   N   R   F   S   G   V   P   D   R   F   S   G   S   G   S>

       300         310         320         330
GGG ACA GAT TTC ACA CTC AAG ATC AGC ACA ATA AAG CCT GAG GAC TTG
 G   T   D   F   T   L   K   I   S   T   I   K   P   E   D   L>

                                                    JK2 (joining
340         350         360         370              380
GGA ATG TAT TAC TGC TTA CAA GGT ACA CAT CAG CCG|TAC ACG TTC GGA
 G   M   Y   Y   C   L   Q   G   T   H   Q   P   Y   T   F   G>

390   region) 400         410  →C_L    420      Kas I   430
                                                 G * G
GGG GGG ACC AAG CTG GAA ATA AAA|CGG GCT GAT GCT GCA CCA ACT GTA
 G   G   T   K   L   E   I   K   R   A   D   A   A   P   T   V>

              3' primer region
  440        450        460        470        480        490
TCCAT CTTCCCACCA TCCAGTAAGC TTGGGAATCC ATATGACTAG TAGATCCTCT

     500        510        520        530
AGAGTCGACC TGCAGGCATG CAAGCTTCCC TATAGTGAGT CGTAT
```

FIG. 3

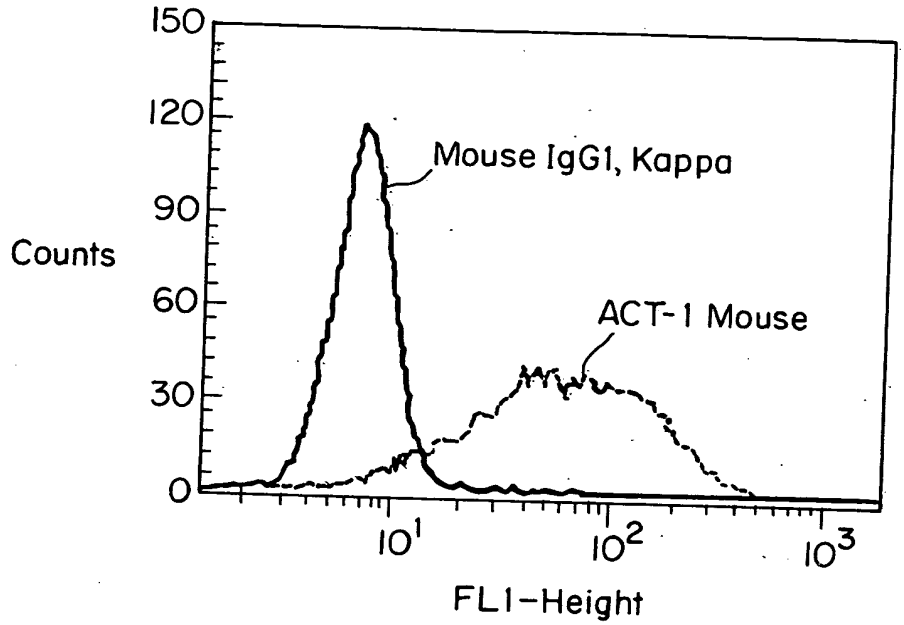

FIG. 4A

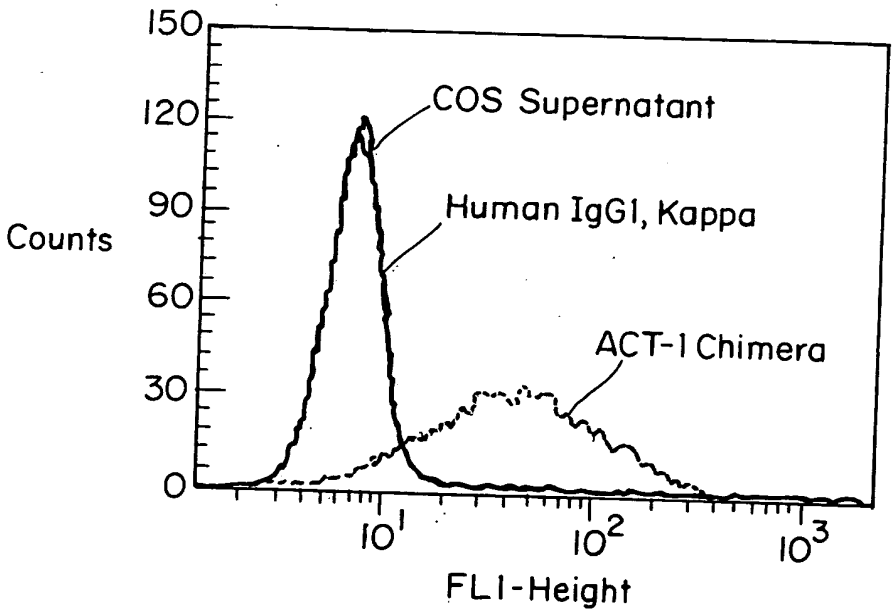

FIG. 4B

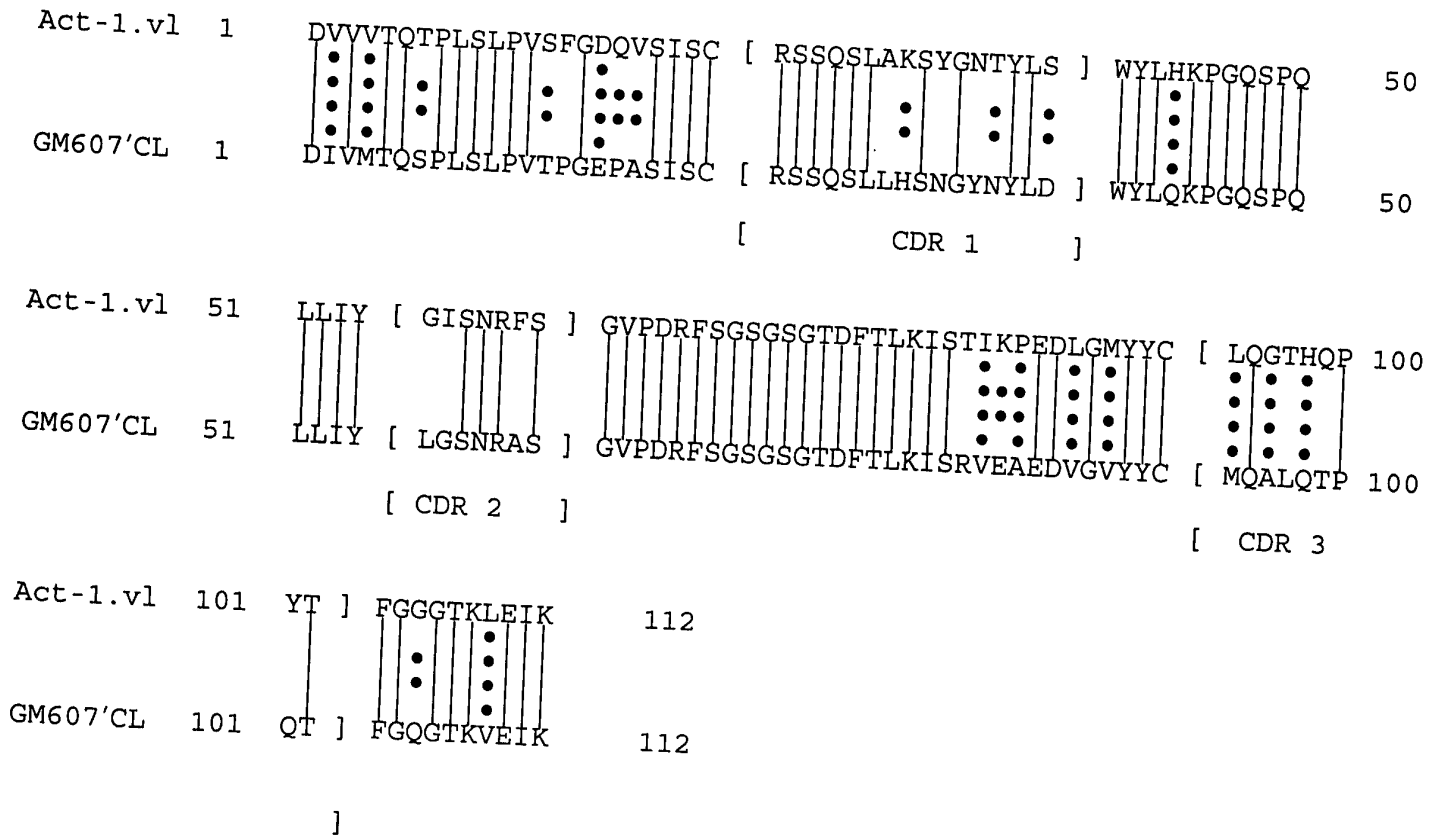

FIG. 5

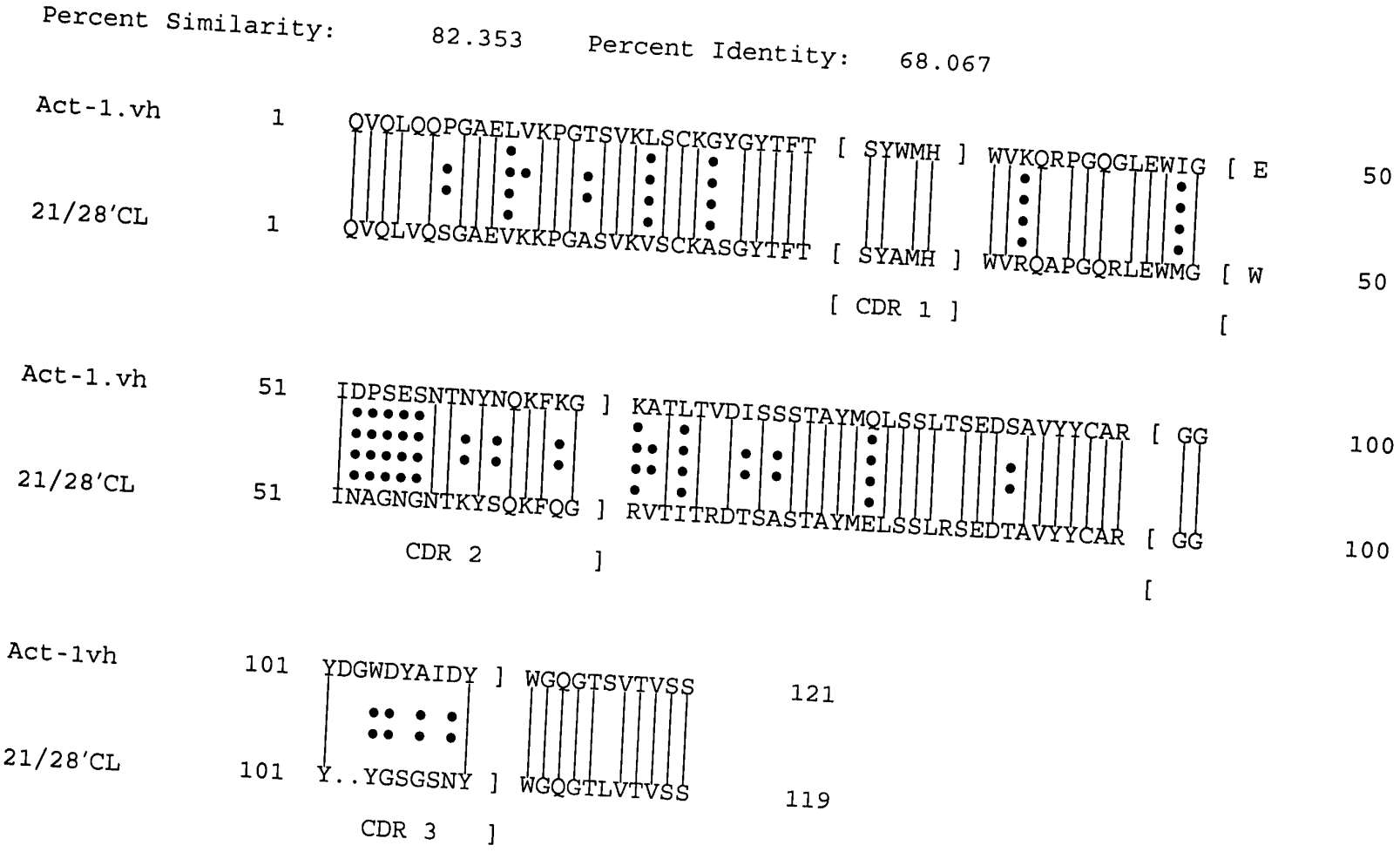

FIG. 6

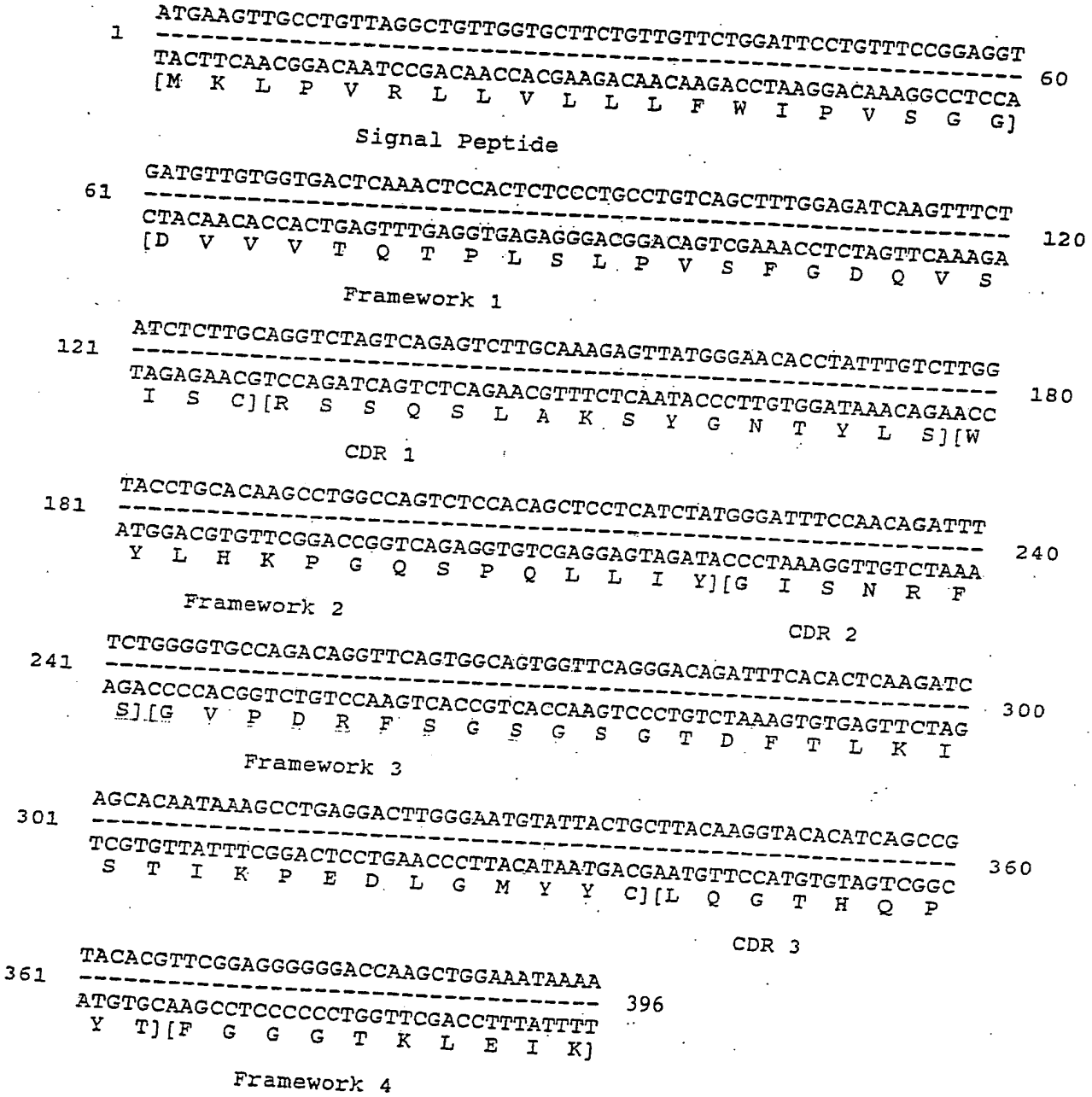

FIG. 7

```
                GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGAGAGCCGGCCTCC
1               ------------------------------------------------------------
                CTATAACACTACTGAGTCAGAGGTGAGAGGGACGGGCAGTGGGGACCTCTCGGCCGGAGG   60
                [D  I  V  M  T  Q  S  P  L  S  L  P  V  T  P  G  E  P  A  S

                                    Framework 1

                ATCTCCTGCAGGTCTAGTCAGAGCCTCCTCCATAGTAATGGATCAAACTATTTGGATTGG
61              ------------------------------------------------------------
                TAGAGGACGTCCAGATCAGTCTCGGAGGAGGTATCATTACCTAGTTTGATAAACCTAACC  120
                 I  S  C][R  S  S  Q  S  L  L  H  S  N  G  Y  N  Y  L  D][W

                                      CDR 1

                TACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCTGATCTATTTGGGTTCTAATCGGGCC
121             ------------------------------------------------------------
                ATGGACGTCTTCGGTCCCGTCAGAGGTGTCGAGGACTAGATAAACCCAAGATTAGCCCGG  180
                 Y  L  Q  K  P  G  Q  S  P  Q  L  L  I  Y][L  G  S  N  R  A

                          Framemwork 2                          CDR 2

                TCCGGGGTCCCTGACAGGTTCAGTGGCAGTGGATCAGGCACAGATTTTACACTGAAAATC
181             ------------------------------------------------------------
                AGGCCCCAGGGACTGTCCAAGTCACCGTCACCTAGTCCGTGTCTAAAATGTGTCTTTTAG  240
                 S][G  V  P  D  R  F  S  G  S  G  S  G  T  D  F  T  L  K  I

                                    Framework 3

241             AGCAGAGTGGAGGCTGAGGATGTTGGGGTTTATTACTGCATGCAAGCTCTACCAACTCCT
                ------------------------------------------------------------
                TCGTCTCACCTCCGACTCCTACAACCCCAAATAATGACGTACGTTCGAGATGGTTGAGGA  300
                 S  R  V  E  A  E  D  V  G  V  Y  Y  C][M  Q  A  L  Q  T  P

                                                      CDR 3

301             CAGACGTTCGGCCAAGGGACCAAGGTGGAAATCAAA
                ------------------------------------
                GTCTGCAAGCCGGTTCCCTGGTTCCACCTTTAGTTT  336
                 Q  T][F  G  Q  G  T  K  V  E  I  K

                          Framework 4
```

FIG. 8

```
                ATGGGATGGAGCTGTATCATCCTCTTCTTGGTATCAACAGCTACAAGTGTCCACTCCCAG
1               ------------------------------------------------------------
                TACCCTACCTCGACATAGTAGGAGAAGAACCATAGTTGTCGATGTTCACAGGTGAGGGTC   60
                 M  G  W  S  C  I  I  L  F  L  V  S  T  A  T  S  V  H  S][Q

                                    Signal Peptide

                GTCCAACTGCAGCAGCCTGGGGCTGAGCTTGTGAAGCCTGGGACTTCAGTGAAGCTGTCC
61              ------------------------------------------------------------
                CAGGTTGACGTCGTCGGACCCCGACTCGAACACTTCGGACCCTGAAGTCACTTCGACAGG  120
                 V  Q  L  Q  Q  P  G  A  E  L  V  K  P  G  T  S  V  K  L  S

                                    Framework 1

                TGCAAGGGTTATGGCTACACCTTCACCAGCTACTGGATGCACTGGGTGAAGCAGAGGCCT
121             ------------------------------------------------------------
                ACGTTCCCAATACCGATGTGGAAGTGGTCGATGACCTACGTGACCCACTTCGTCTCCGGA  180
                 C  K  G  Y  G  Y  T  F  T][S  Y  W  M  H][W  V  K  Q  R  P

                                                        CDR 1

                GGACAAGGCCTTGAGTGGATCGGAGAGATTGATCCTTCTGAGAGTAATACTAACTACAAT
181             ------------------------------------------------------------
                CCTGTTCCGGAACTCACCTAGCCTCTCTAACTAGGAAGACTCTCATTATGATTGATGTTA  240
                 G  Q  G  L  E  W  I  G][E  I  D  P  S  E  S  N  T  N  Y  N

                    Framework 2                         CDR 2

                CAAAAATTCAAGGGCAAGGCCACATTGACTGTAGACATTTCCTCCAGCACAGCCTACATG
241             ------------------------------------------------------------
                GTTTTTAAGTTCCCGTTCCGGTGTAACTGACATCTGTAAAGGAGGTCGTGTCGGATGTAC  300
                 Q  K  F  K  G][K  A  T  L  T  V  D  I  S  S  S  T  A  Y  M

                                    Framework 3

                CAGCTCAGCAGCCTGACATCTGAGGACTCTGCGGTCTACTATTGTGCAAGAGGGGGTTAC
301             ------------------------------------------------------------
                GTCGAGTCGTCGGACTGTAGACTCCTGAGACGCCAGATGATAACACGTTCTCCCCCAATG  360
                 Q  L  S  S  L  T  S  E  D  S  A  V  Y  Y  C  A  R][G  G  Y

                GACGGATGGGACTATGCTATTGACTACTGGGGTCAAGGCACCTCAGTCACCGTCTCCTCA
361             ------------------------------------------------------------
                CTGCCTACCCTGATACGATAACTGATGACCCCAGTTCCGTGGAGTCAGTGGCAGAGGAGT  420
                 D  G  W  D  Y  A  I  D  Y][W  G  Q  G  T  S  V  T  V  S  S]

                    CDR 3                               Framework 4
```

FIG. 9

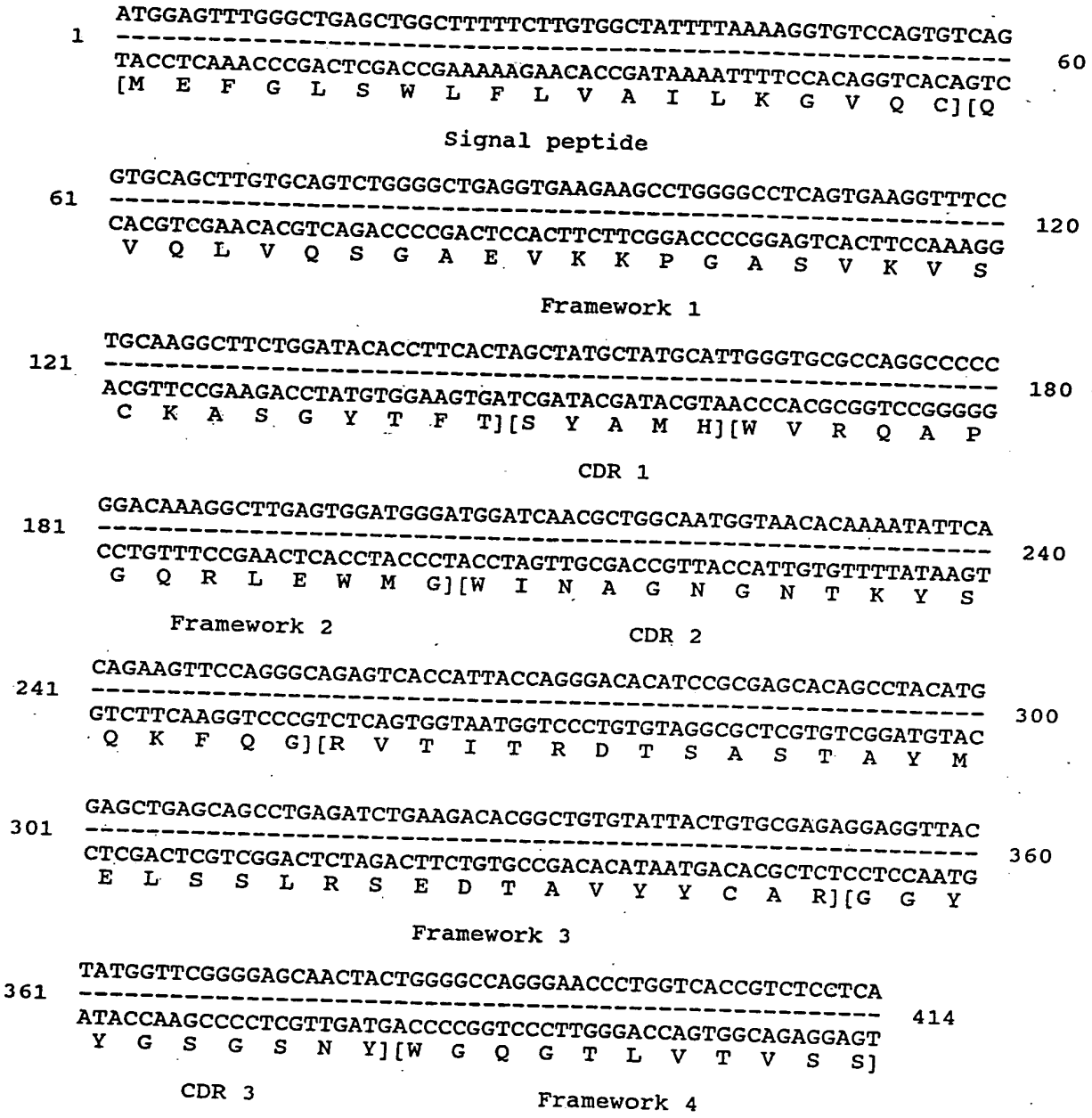

FIG. 10

```
          10          20          30          40
     *    *     *     *     *     *     *     *     *
ATG AAA TGC ACC TGG GTC ATT CTC TTC TTG GTA TCA ACA GCT ACA AGT
 M   K   C   T   W   V   I   L   F   L   V   S   T   A   T   S>
           Single peptide cleavage site
50        | 60          70          80          90
 *     *  |  *     *  *|Spe I*     *     *     *     *     *
GTC CAC TCC↓CAG GTC CAA CTA GTG CAG TCT GGG GCT GAG GTT AAG AAG
 V   H   S   Q   V   Q|  L   V   Q   S   G   A   E   V   K   K >
                      |
  100         110         120         130         140
    *     *     *     *     *     *     *     *     *
CCT GGG GCT TCA GTG AAG GTG TCC TGC AAG GGT TCT GGC TAC ACC TTC
 P   G   A   S   V   K   V   S   C   K   G   S   G   Y   T   F>
                                                        Xba I
    150         160         170         180         190
*     *     *     *     *     *     *     *     *     |  *
ACC AGC TAC TGG ATG CAT TGG GTG AGG CAG GCG CCT GGC CAA CGT CTA
 T   S   Y   W   M   H   W   V   R   Q   A   P   G   Q   R|  L>
       200         210         220         230         240
 *     *     *     *     *     *     *     *     *     *     *
GAG TGG ATC GGA GAG ATT GAT CCT TCT GAG AGT AAT ACT AAC TAC AAT
 E   W   I   G   E   I   D   P   S   E   S   N   T   N   Y   N>
           250         260         270         280     Nhe I
     *     *     *     *     *     *     *     *     *
CAA AAA TTC AAG GGA CGC GTC ACA TTG ACT GTA GAC ATT TCC|GCT AGC|
 Q   K   F   K   G   R   V   T   L   T   V   D   I   S |  A   S>|
   290         300         310         320         330
 *     *     *     *     *     *     *     *     *     *
ACA GCC TAC ATG GAG CTC AGC AGC CTG AGA TCT GAG GAC ACT GCG GTC
 T   A   Y   M   E   L   S   S   L   R   S   E   D   T   A   V>
  340         350         360         370         380
    *     *     *     *     *     *     *     *     *
TAC TAT TGT GCA AGA GGG GGT TAC GAC GGA TGG GAC TAT GCT ATT GAC
 Y   Y   C   A   R   G   G   Y   D   G   W   D   Y   A   I   D>
    390         400  BstE II 410         420  Constant430
*     *     *     *     *     *     *     *|     *region *
TAC TGG GGT CAA GGC ACC CTG GTC ACC|GTC TCC TCA|GCC TCC ACC AAG
 Y   W   G   Q   G   T   L|  V   T |  V   S   S |  A   S   T   K>
       440         450         460         470         480
 *     *     *     *     *     *     *     *     *     *
GGC CCA TCG GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG
 G   P   S   V   F   P   L   A   P   S   S   K   S   T   S   G>
    490         500         510         520
    *     *     *     *     *     *     *     *     *Age I
GGC ACA GCG GCC CTG GGC TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG
 G   T   A   A   L   G   C   L   V   K   D   Y   F   P   E|  P>
530         540
 *|    *     *
GTG ACG GTG TCG
 V|  T   V   S>
```

FIG. 11

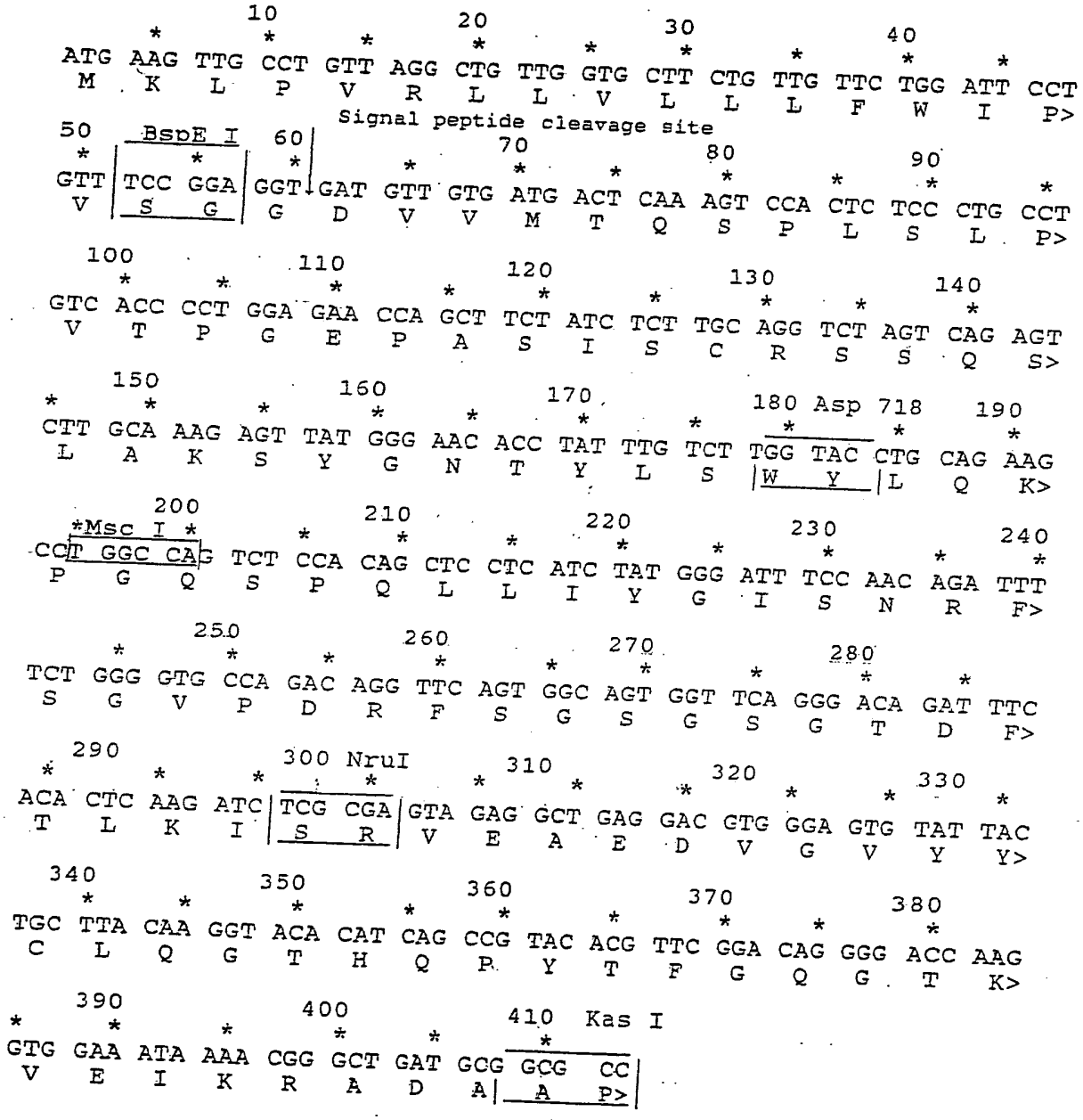

FIG. 12

LIGHT CHAIN OLIGOS: DOUBLE STRAND FRAGMENTS

L1 5'- TTT CCG GAG GTG ATG TTG TGA TGA CTC AAA GTC CAC TCT CCC TGC CTG TCA CCC CTG GAG AAC CAG CTT CTA TCT CTT GCA GGT CTA GTC AGA G

LA

L2 5'- ACT GGC CAG GCT TCT GCA GGT ACC AAG ACA AAT AGG TGT TCC CAT AAC TCT TTG CAA GAC TCT GAC TAG ACC TGC AAG AGA TAG AAG CTG GTT C

L3 5'- CCT GGC CAG TCT CCA CAG CTC CTC ATC TAT GGG ATT TCC AAC AGA TTT TCT GGG GTG CCA GAC AGG TTC AGT GGC AGT GGT TC

LB

L4 5'- ACT CGC GAG ATC TTG AGT GTG AAA TCT GTC CCT GAA CCA CTG CCA CTG AAC CTG TCT GGC ACC CCA GAA AAT CTG TTG GAA ATC

L5 5'- TCT CGC GAG TAG AGG CTG AGG ACG TGG GAG TGT ATT ACT GCT TAC AAG GTA CAC ATC AGC CGT ACA C

LC

L6 5'- ATG GCG CCG CAT CAG CCC GTT TTA TTT CCA CCT TGG TCC CCT GTC CGA ACG TGT ACG GCT GAT GTG TAC CTT GTA AGC AGT AAT AC

HEAVY CHAIN OLIGOS DOUBLE STRAND FRAGMENT

H1 5'- ATA AGC TTC GCC ATG AAA TGC ACC TGG GTC ATT CTC TTC TTG GTA TCA ACA GCT ACA AGT GTC CAC TCC CAG GTC CAA CTA GTG CAC CGG TTA

HA

H2 5'- TAA CCG GTG CAC TAG TTG GAC CTG GGA GTG GAC ACT TGT AGC TGT TGA TAC CAA GAA GAG AAT GAC CCA GGT GCA TTT CAT GGC GAA GCT TAT

H3 5'- CAA CTA GTG CAG TCT GGG GCT GAG GTT AAG AAG CCT GGG GCT TCA GTG AAG GTG TCC TGC AAG GGT TCT GGC TAC ACC TTC ACC AGC

HB

H4 5'- TAA CCG GTA CTC TAG ACG TTG GCC AGG CGC CTG CCT CAC CCA ATG CAT CCA GTA GCT GGT GAA GGT GTA GCC AGA ACC CTT GCA GGA C

H5 5'- CGT CTA GAG TGG ATC GGA GAG ATT GAT CCT TCT GAG AGT AAT ACT AAC TAC AAT CAA AAA TTC AAG GGA CGC GTC A

HC

H6 5'- TAA CCG GTG TGC TAG CGG AAA TGT CTA CAG TCA ATG TGA CGC GTC CCT TGA ATT TTT GAT TGT AGT TAG TAT TAC T

H7 5'- CCG CTA GCA CAG CCT ACA TGG AGC TCA GCA GCC TGA GAT CTG AGG ACA CTG CGG TCT ACT ATT GTG CAA GAG GGG GTT ACG ACG GAT G

HD

H8 5'- TCA CCG GTG CGG TGA CCA GGG TGC CTT GAC CCC AGT AGT CAA TAG CAT AGT CCC ATC CGT CGT AAC CCC CTC TTG CAC AAT AGT AGA C

H9 5'- CTG GTC ACC GTC TCC TCA GCC TCC ACC AAG GGC CCA TCG GTC TTC CCC CTG GCA CCC TCC TCC AAG AGC ACC TCT GGG GGC ACA G

HE

H10 5'- TCA CCG GTT CGG GGA AGT AGT CCT TGA CCA GGC AGC CCA GGG CCG CTG TGC CCC CAG AGG TGC TCT TGG AGG AGG GTG CCA GGG G

FIG. 13

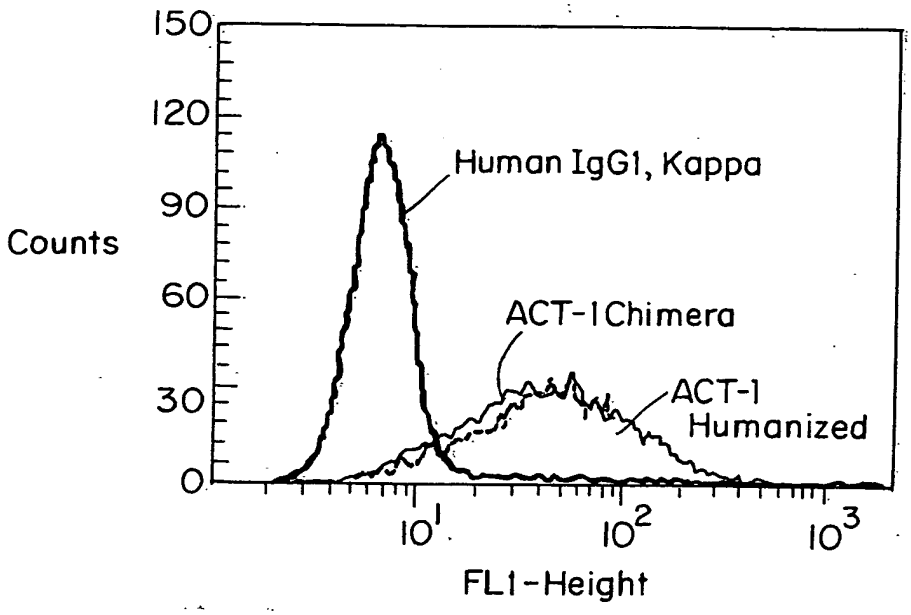

FIG. 14

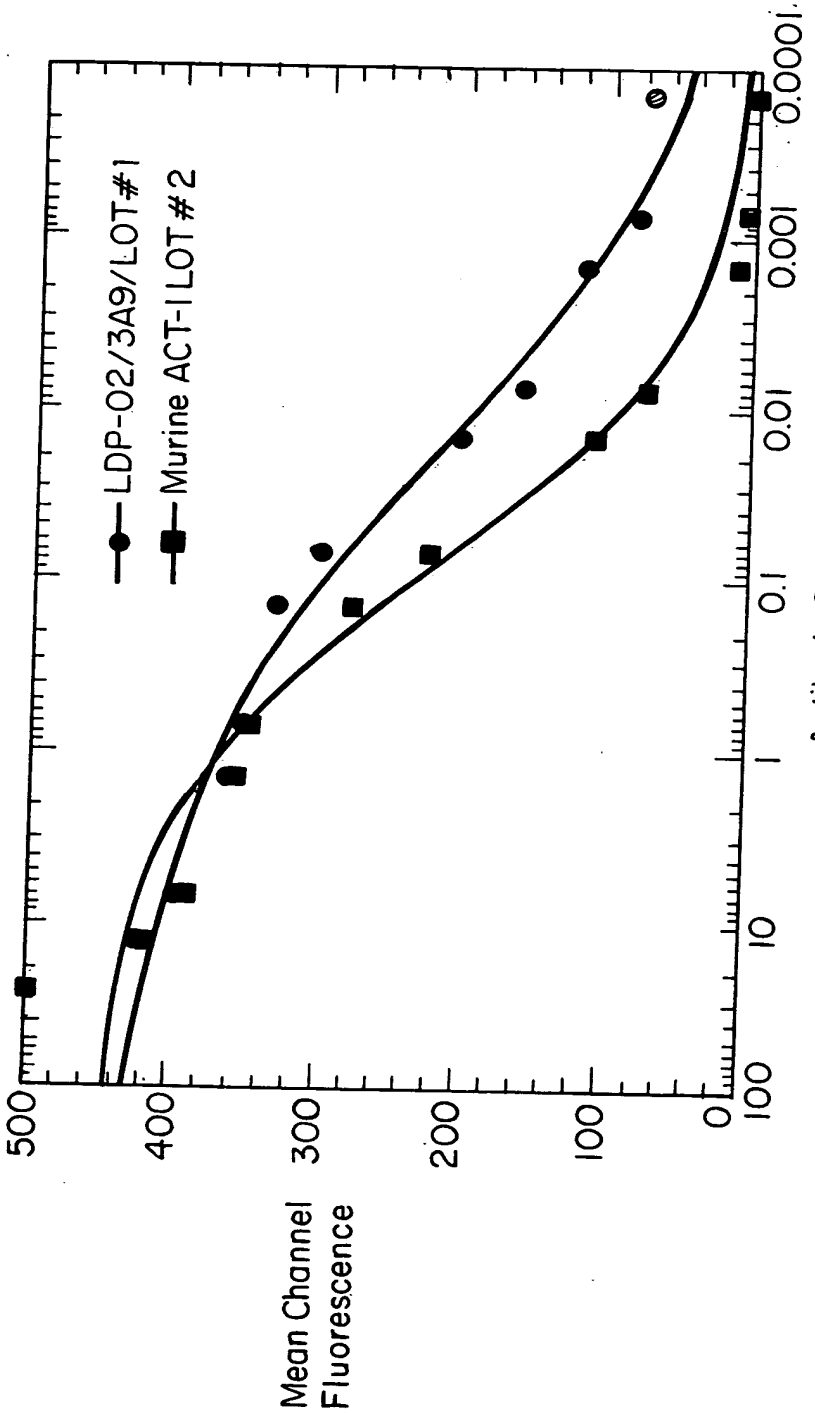

FIG. 15

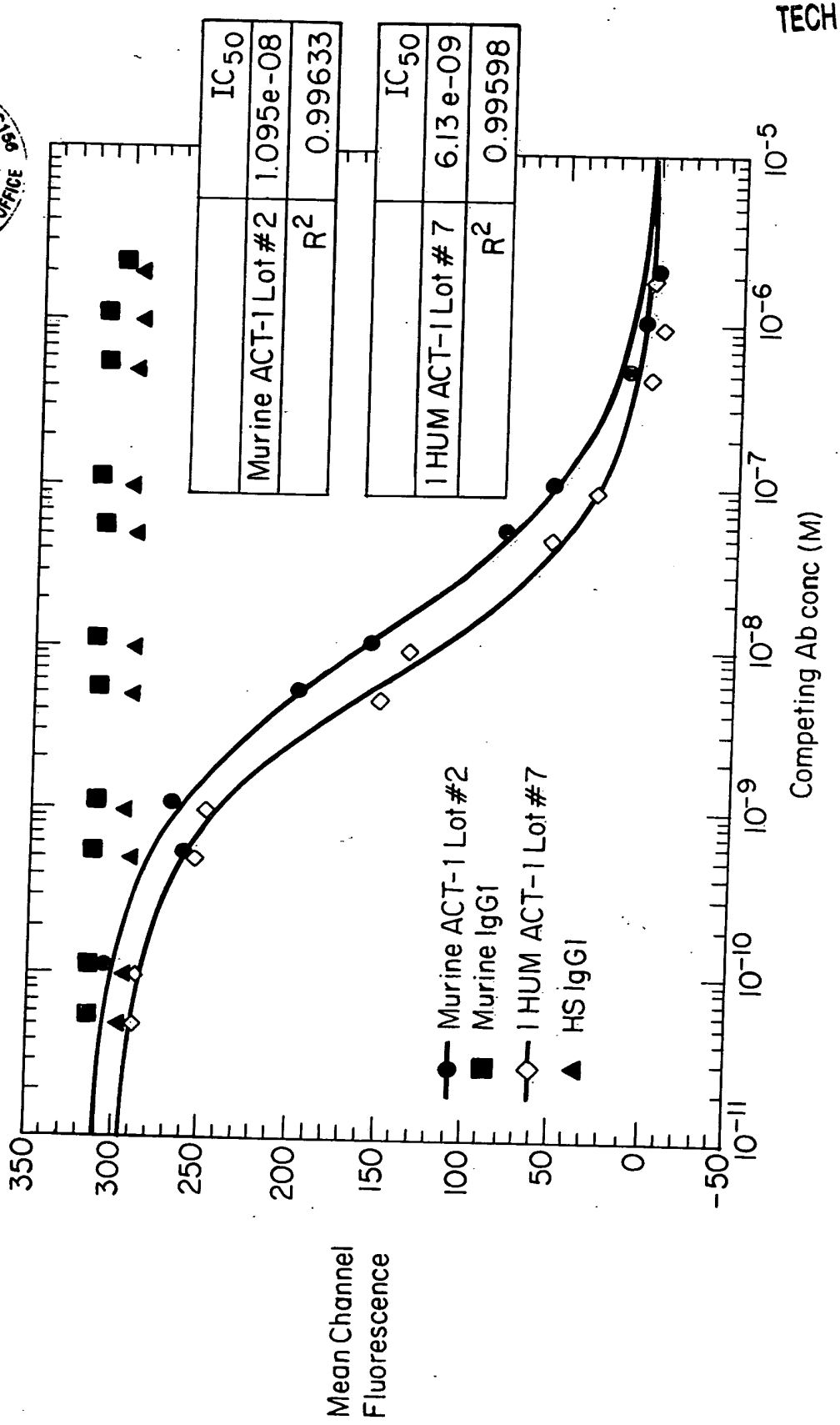

FIG. 16

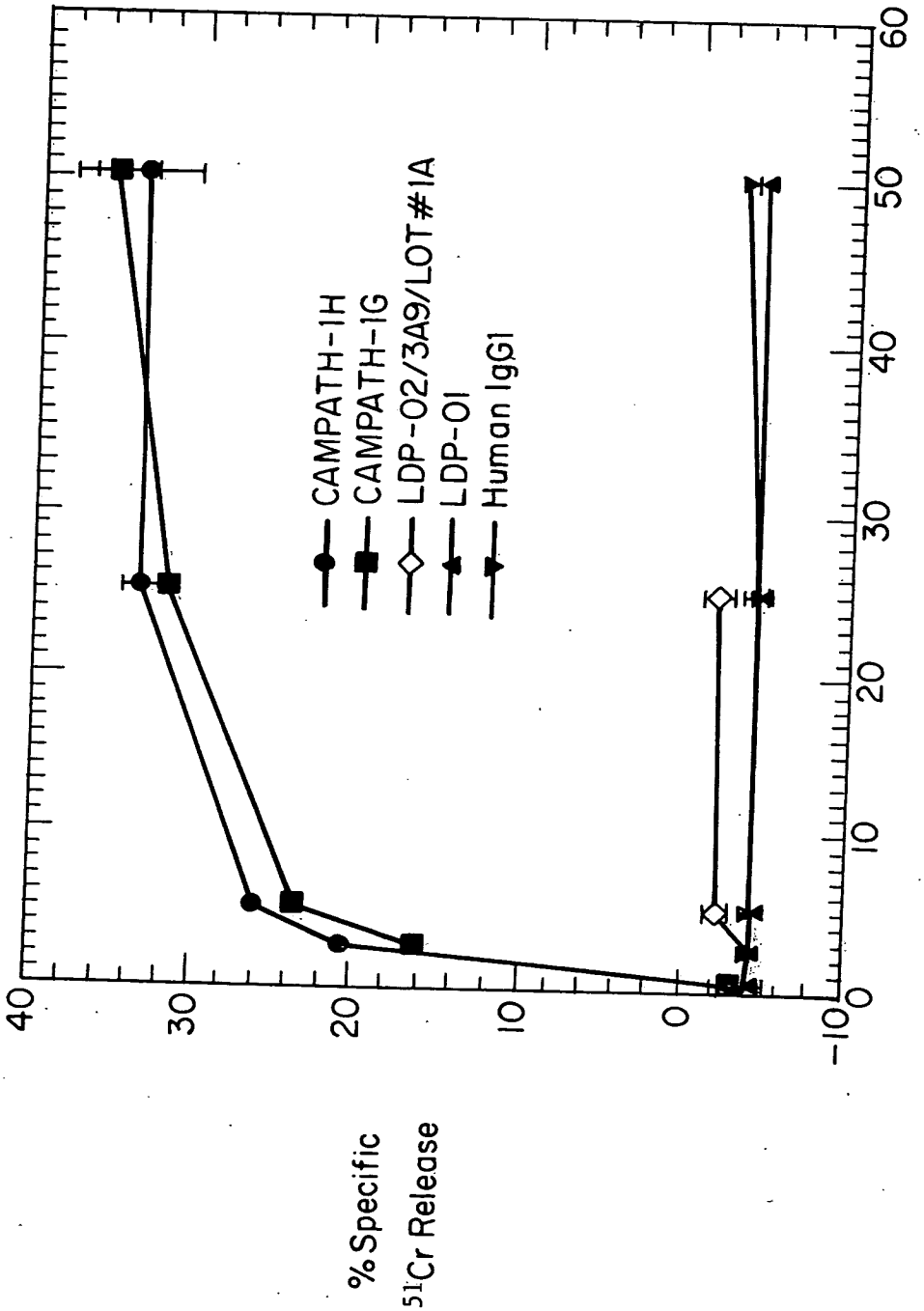

FIG. 17

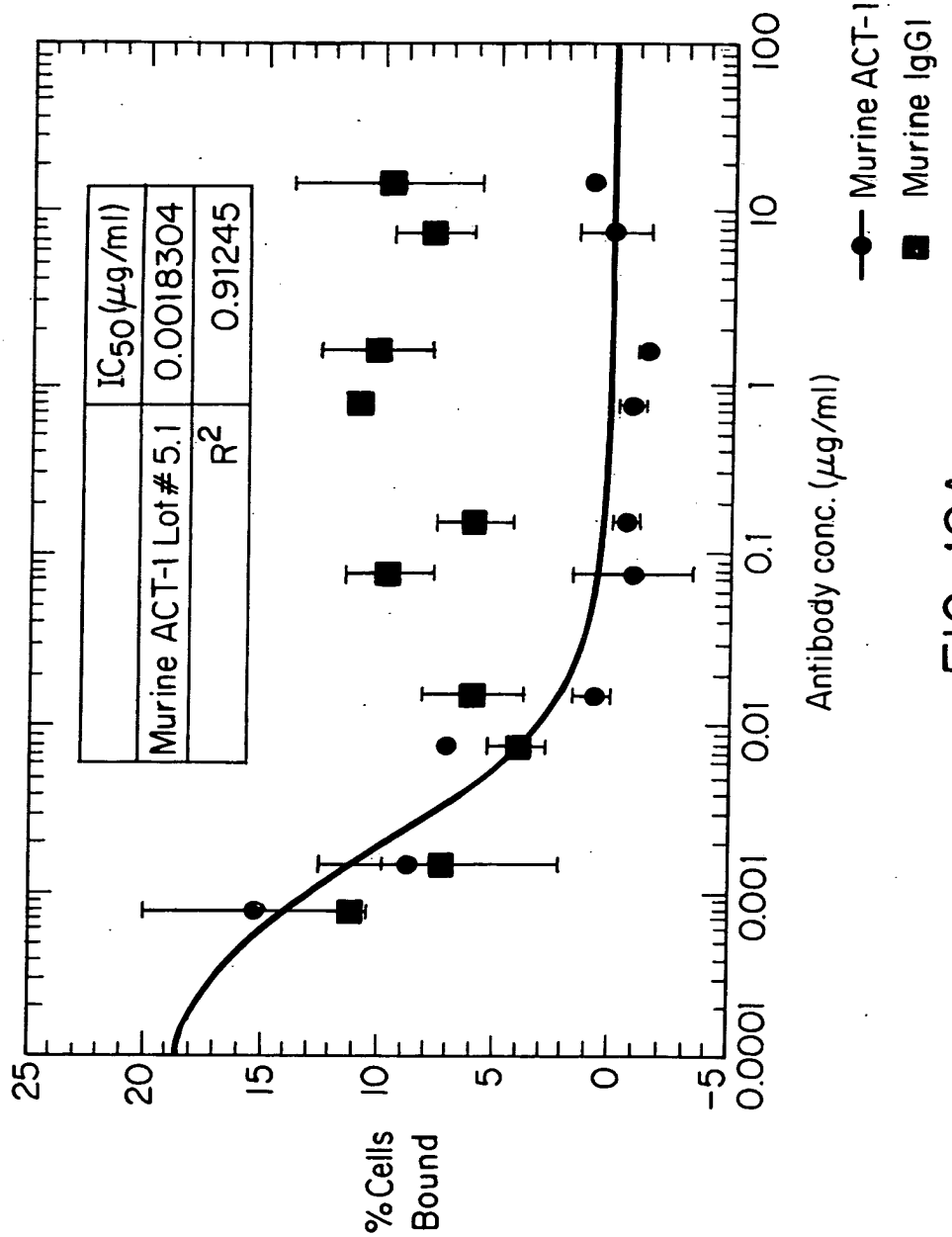

FIG. 18A

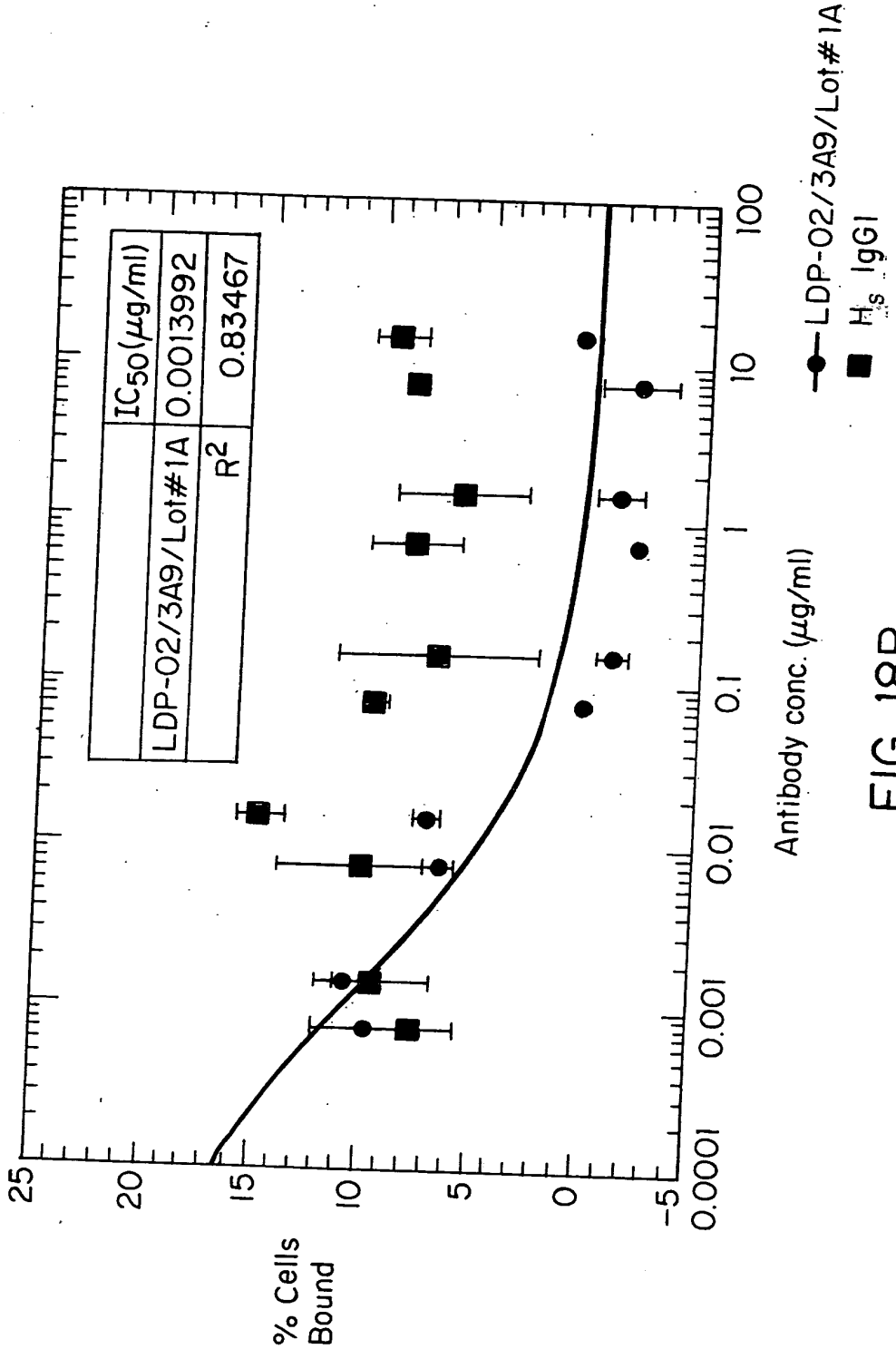

FIG. 18B

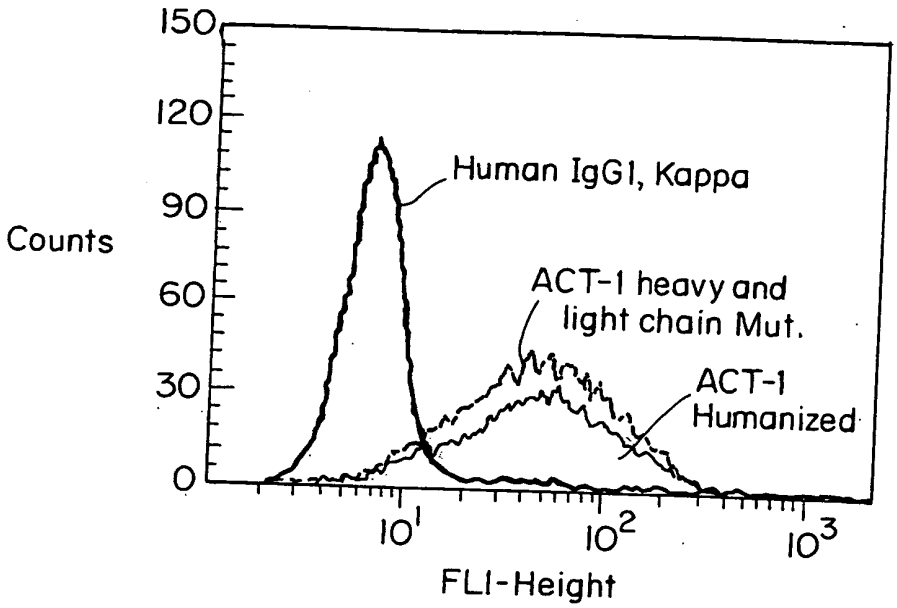

FIG. 19